Application # Search

L5 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1333982 HCAPLUS
DOCUMENT NUMBER: 144:70109
ENTRY DATE: Entered STN: 22 Dec 2005
TITLE: Preparation of peptide boronic acids as anticoagulants
INVENTOR(S): Combe-Marzelle, Sophie Marie; Kennedy, Anthony James; Allen, Graham Douglas; Withington, Roger; Krimmer, Dieter
PATENT ASSIGNEE(S): Trigen Limited, Switz.
SOURCE: U.S. Pat. Appl. Publ., 75 pp., Cont.-in-part of U.S. Ser. No. 937,181.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K038-05
SECONDARY: A61K031-69
US PATENT CLASSIF.: 514018000; 514064000
CLASSIFICATION: 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 29, 63
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005282757	A1	20051222	US 2005-78097	20050309 <--
AU 2003263328	A1	20040329	AU 2003-263328	20030909
AU 2003263333	A1	20040329	AU 2003-263333	20030909
AU 2003263343	A1	20040329	AU 2003-263343	20030909
US 2004138175	A1	20040715	US 2003-658971	20030909 <--
US 2004147453	A1	20040729	US 2003-659179	20030909
EP 1466916	A1	20041013	EP 2004-76510	20030909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
EP 1466917	A1	20041013	EP 2004-76521	20030909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014450	A	20050726	BR 2003-14450	20030909
BR 2003014518	A	20050726	BR 2003-14518	20030909
EP 1561466	A2	20050810	EP 2004-76548	20030909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005288253	A1	20051229	US 2003-659178	20030909
JP 2006503903	T2	20060202	JP 2004-569794	20030909
US 2005119226	A1	20050602	US 2004-937181	20040908
US 2005176651	A1	20050811	US 2004-937854	20040908 <--
PRIORITY APPLN. INFO.:			GB 2002-20764	A 20020909
			GB 2002-20822	A 20020909
			GB 2003-7817	A 20030404
			GB 2003-11237	A 20030516
			GB 2003-15691	A 20030704
			US 2003-501718P	P 20030909
			US 2003-658971	A2 20030909 <--
			US 2003-659178	A2 20030909
			US 2003-659179	A2 20030909
			US 2004-937181	A2 20040908
			US 2004-937854	A2 20040908
			US 2003-485786P	P 20030708

EP 2003-255590	A3	20030909
WO 2003-GB3883	W	20030909
WO 2003-GB3887	W	20030909
WO 2003-GB3897	W	20030909

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2005282757	ICM	A61K038-05
	ICS	A61K031-69
	INCL	514018000; 514064000
	IPCI	A61K0038-05 [ICM,7]; A61K0031-69 [ICS,7]
	NCL	514/018.000; 514/064.000 <--
AU 2003263328	IPCI	A61K0031-69 [ICM,7]; C07F0005-02 [ICS,7]; C07D0207-08 [ICS,7]
AU 2003263333	IPCI	A61K0031-69 [ICM,7]; C07D0207-08 [ICS,7]; C07F0005-02 [ICS,7]
AU 2003263343	IPCI	A61K0031-69 [ICM,7]; C07F0005-02 [ICS,7]; C07D0207-08 [ICS,7]
US 2004138175	IPCI	A61K0031-69 [ICM,7]
	IPCR	A61K0031-69 [I,A]; A61K0031-69 [I,C]; A61K0038-04 [I,A]; A61K0038-04 [I,C]; C07F0005-00 [I,C]; C07F0005-02 [I,A]
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EP 1466916	IPCI	C07F0005-02 [ICM,7]
	ECLA	A61K031/69; C07F005/02C; C07K005/06A2+H; C07K005/06T
EP 1466917	IPCI	C07F0005-02 [ICM,7]; C07F0005-04 [ICS,7]
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BR 2003014450	IPCI	A61K0031-69 [ICM,7]; C07F0005-02 [ICS,7]; C07D0207-08 [ICS,7]
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BR 2003014518	IPCI	A61K0031-69 [ICM,7]; C07F0005-02 [ICS,7]; C07D0207-08 [ICS,7]
EP 1561466	IPCI	A61K0031-69 [ICM,7]; C07F0005-02 [ICS,7]; C07D0207-08 [ICS,7]
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US 2005288253	IPCI	C07F0005-02 [ICM,7]; A61K0031-69 [ICS,7]
	NCL	514/064.000; 562/007.000
JP 2006503903	IPCI	C07K0005-06 [I,A]; A61K0009-48 [I,A]; A61K0045-00 [I,A]; A61P0007-02 [I,A]; A61P0009-10 [I,A]; A61P0013-12 [I,A]; A61P0043-00 [I,A]; C07K0005-065 [I,A]; A61K0038-00 [I,A]; C12N0009-99 [N,A]
	FTERM	4C076/AA45; 4C076/AA60; 4C076/AA94; 4C076/AA95; 4C076/BB01; 4C076/CC11; 4C076/CC14; 4C076/CC17; 4C076/EE42; 4C076/FF24; 4C076/FF27; 4C076/FF31; 4C084/AA02; 4C084/AA03; 4C084/AA06; 4C084/AA07; 4C084/AA19; 4C084/BA14; 4C084/BA23; 4C084/BA33; 4C084/CA59; 4C084/DC35; 4C084/MA52; 4C084/NA14; 4C084/ZA36; 4C084/ZA54; 4C084/ZA81; 4C084/ZC20; 4H045/AA10; 4H045/AA20; 4H045/AA30; 4H045/BA11; 4H045/BA50; 4H045/DA56; 4H045/EA24; 4H045/FA10; 4H045/GA05
US 2005119226	IPCI	C07F0005-02 [ICM,7]; A61K0031-69 [ICS,7]
	IPCR	C07F0005-00 [I,C]; C07F0005-02 [I,A]

	NCL	514/064.000
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	IPCR	A61K0031-69 [I,A]; A61K0031-69 [I,C]; A61K0038-04 [I,A]; A61K0038-04 [I,C]; C07F0005-00 [I,C]; C07F0005-02 [I,A]; C07K0005-00 [I,C]; C07K0005-04 [I,A]
	NCL	514/019.000 <--

OTHER SOURCE(S): MARPAT 144:70109

ABSTRACT:
The invention relates to peptide boronic acids and their pharmaceutically-acceptable salts and prodrugs which are useful for preventing thrombosis where rapid onset and/or rapid offset of anticoagulation is required. The boronic acids have a neutral thrombin P1 domain linked to a hydrophobic moiety capable of binding to the thrombin S2 and S3 subsites. Thus, Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)2 (TRI 50c; Cbz = benzyloxycarbonyl; Mpg = 3-methoxypropylglycine residue) and several salts were prepared The activity of TRI 50c magnesium salt in a thrombin amidolytic assay is shown in a figure.

SUPPL. TERM: peptide boronic acid prepn anticoagulant

INDEX TERM: Tripeptides
ROLE: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(boronic; preparation of peptide boronic acids as anticoagulants)

INDEX TERM: Anticoagulants
Thrombosis
(preparation of peptide boronic acids as anticoagulants)

INDEX TERM: **864466-86-4P 864466-94-4P**
871575-98-3P 871575-99-4P
871576-00-0P 871576-01-1P
871576-02-2P 871576-04-4P
871576-05-5P 871576-06-6P
871576-08-8P 871576-12-4P
ROLE: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide boronic acids as anticoagulants)

INDEX TERM: 76-09-5, Pinacol 111-42-2, Diethanolamine, reactions
121-43-7, Trimethyl borate 17460-56-9
36215-07-3, 1-Chloro-3-methoxypropane **162854-90-2**
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptide boronic acids as anticoagulants)

INDEX TERM: 54759-60-3P **162854-89-9P 162990-46-7P**
667917-13-7P 667917-14-8P
667935-30-0P 864466-81-9P **864466-82-0P**
864466-83-1P 864466-85-3P 864466-91-1P
864466-92-2P **864466-93-3P 871576-03-3P**
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide boronic acids as anticoagulants)

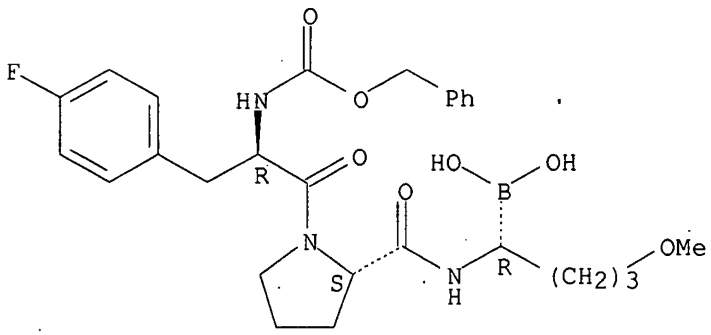
IT **864466-86-4P 864466-94-4P 871575-98-3P**
871575-99-4P 871576-00-0P 871576-01-1P
871576-02-2P 871576-04-4P 871576-05-5P
871576-06-6P 871576-08-8P 871576-12-4P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptide boronic acids as anticoagulants)

RN 864466-86-4 HCAPLUS

CN L-Prolinamide, 4-fluoro-N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, monosodium salt (9CI) (CA INDEX NAME)

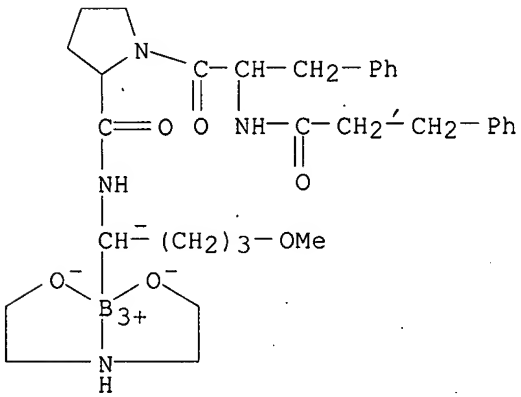
Absolute stereochemistry.



● Na

RN 864466-94-4 HCAPLUS

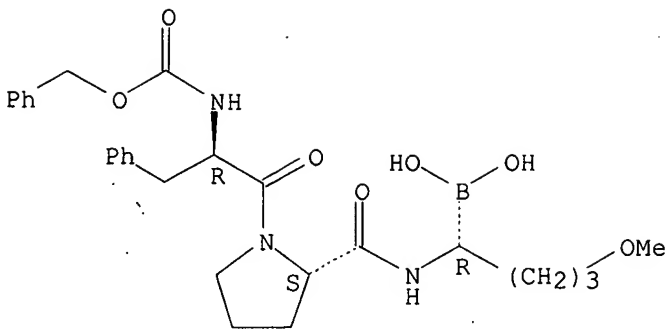
CN Boron, [[2,2'-(imino-κN)bis[ethanolato-κO]](2-)][(1R)-4-methoxy-1-[[N-(1-oxo-3-phenylpropyl)-D-phenylalanyl-L-prolyl]amino]butyl-κC]-, (T-4)- (9CI) (CA INDEX NAME)



RN 871575-98-3 HCAPLUS

CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, monosodium salt (9CI) (CA INDEX NAME)

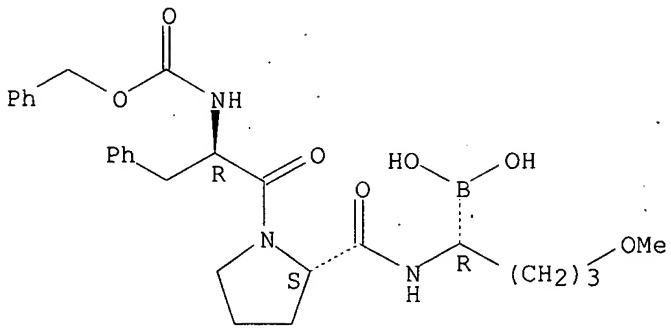
Absolute stereochemistry.



● Na

RN 871575-99-4 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, calcium salt (2:1) (9CI) (CA INDEX NAME)

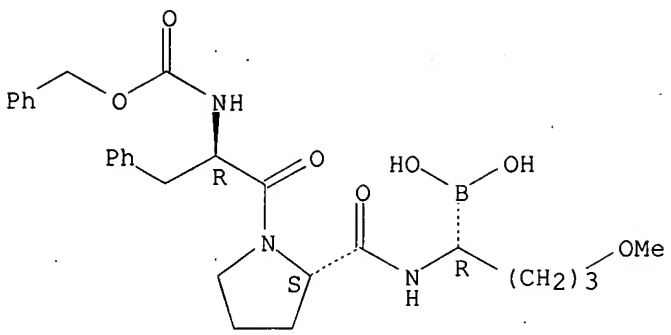
Absolute stereochemistry.



●1/2 Ca

RN 871576-00-0 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, monolithium salt (9CI) (CA INDEX NAME)

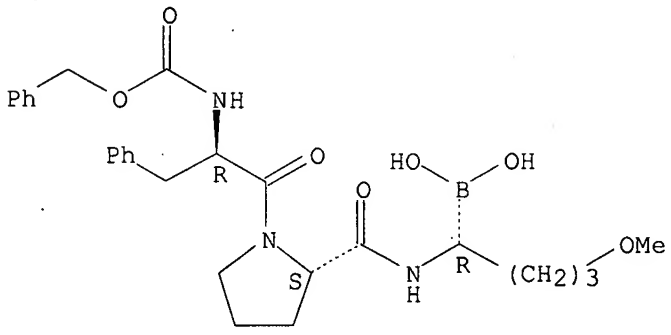
Absolute stereochemistry.



● Li

RN 871576-01-1 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, monopotassium salt (9CI) (CA INDEX NAME)

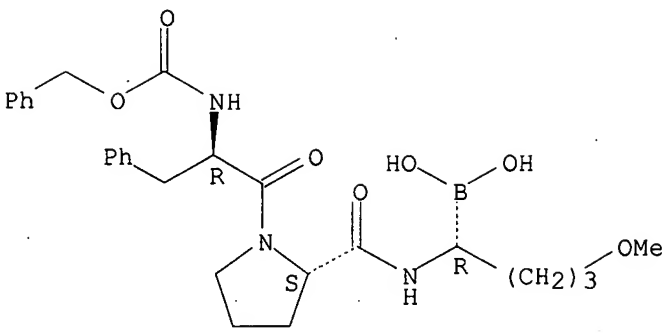
Absolute stereochemistry.



● K

RN 871576-02-2 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, zinc salt (2:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



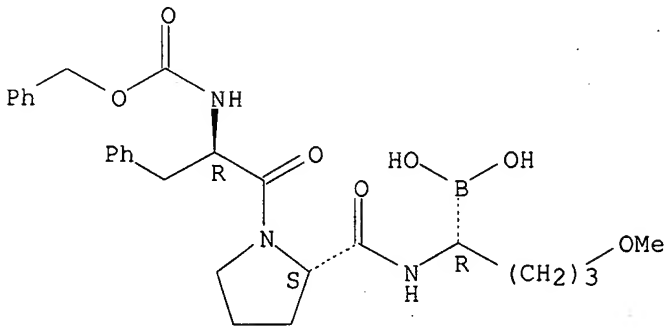
●1/2 Zn

RN 871576-04-4 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, compd. with L-arginine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 871576-03-3
CMF C27 H36 B N3 O7

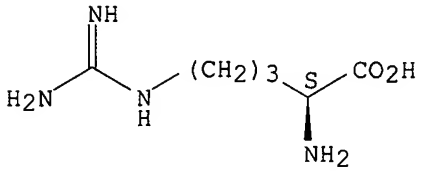
Absolute stereochemistry.



CM 2

CRN 74-79-3
CMF C6 H14 N4 O2

Absolute stereochemistry.

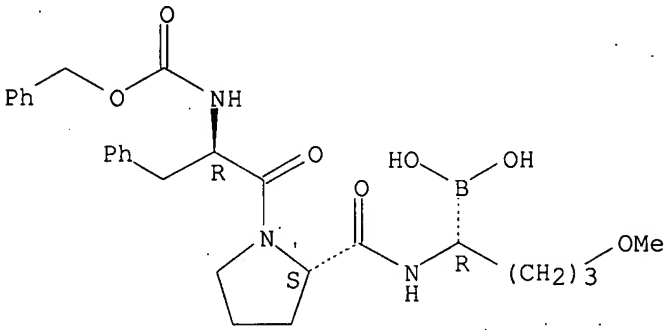


RN 871576-05-5 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, compd. with L-lysine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 871576-03-3
CMF C27 H36 B N3 O7

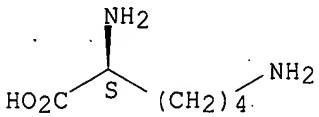
Absolute stereochemistry.



CM 2

CRN 56-87-1
CMF C6 H14 N2 O2

Absolute stereochemistry.

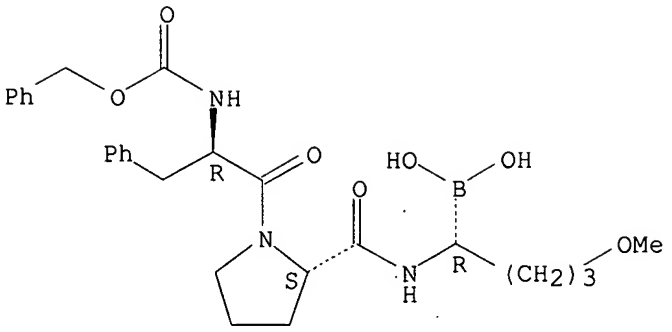


RN 871576-06-6 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, compd. with 1-deoxy-1-(methylamino)-D-glucitol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 871576-03-3
CMF C27 H36 B N3 O7

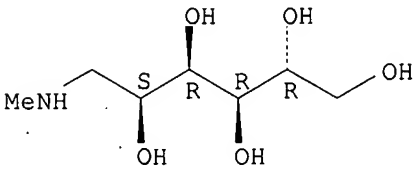
Absolute stereochemistry.



CM 2

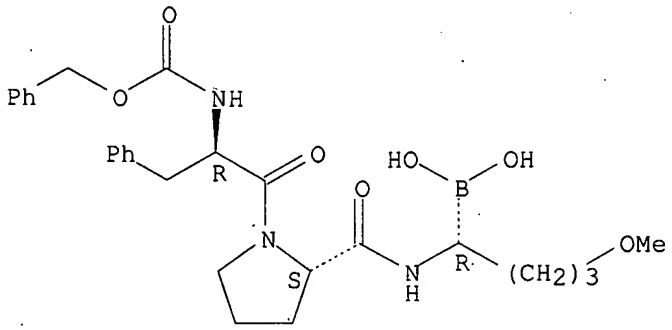
CRN 6284-40-8
CMF C7 H17 N O5

Absolute stereochemistry.



RN 871576-08-8 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, magnesium salt (2:1) (9CI) (CA INDEX NAME)

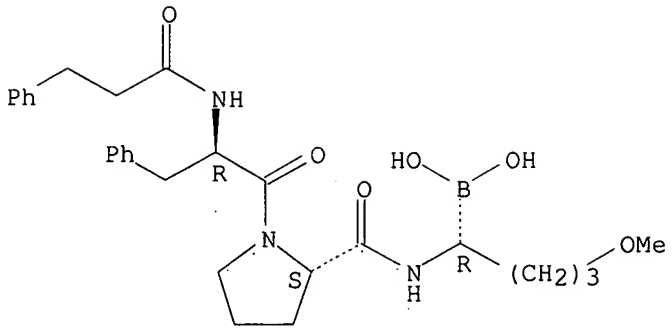
Absolute stereochemistry.



●1/2 Mg

RN 871576-12-4 HCAPLUS
CN L-Prolinamide, N-(1-oxo-3-phenylpropyl)-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● Na

IT **121-43-7**, Trimethyl borate **162854-90-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptide boronic acids as anticoagulants)
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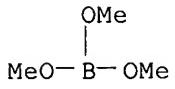
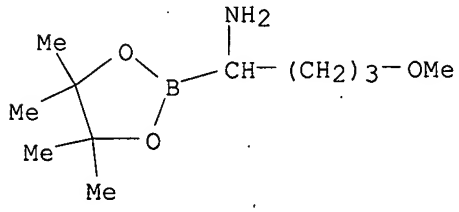
CN Boric acid (H3BO3), trimethyl ester (8CI, 9CI) (CA INDEX NAME)

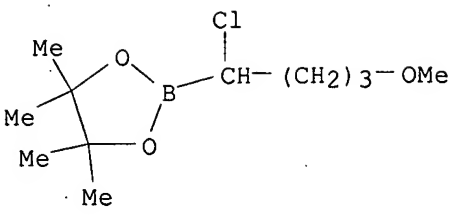


RN 162854-90-2 HCAPLUS
CN 1,3,2-Dioxaborolane-2-methanamine, α-(3-methoxypropyl)-4,4,5,5-tetramethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **162854-89-9P 162990-46-7P 667917-13-7P**
667917-14-8P 667935-30-0P 864466-82-0P
864466-83-1P 864466-93-3P 871576-03-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide boronic acids as anticoagulants)
RN 162854-89-9 HCAPLUS
CN 1,3,2-Dioxaborolane, 2-(1-chloro-4-methoxybutyl)-4,4,5,5-tetramethyl- (9CI) (CA INDEX NAME)



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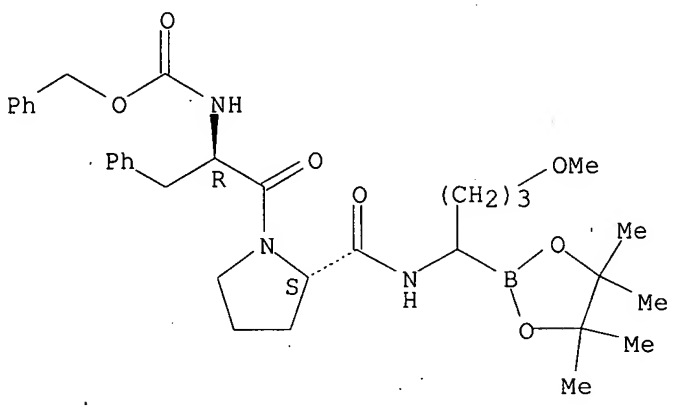
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[4-methoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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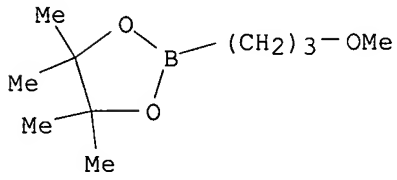
CN 1,3,2-Dioxaborolane, 2-(3-methoxypropyl)-4,4,5,5-tetramethyl- (9CI) (CA INDEX NAME)



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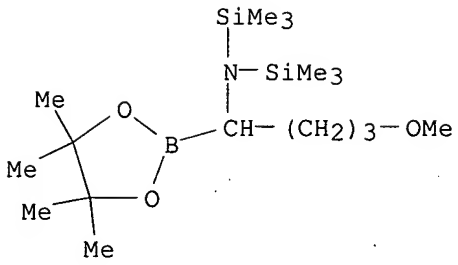
CN 1,3,2-Dioxaborolane-2-methanamine, α-(3-methoxypropyl)-4,4,5,5-tetramethyl-N,N-bis(trimethylsilyl)- (9CI) (CA INDEX NAME)



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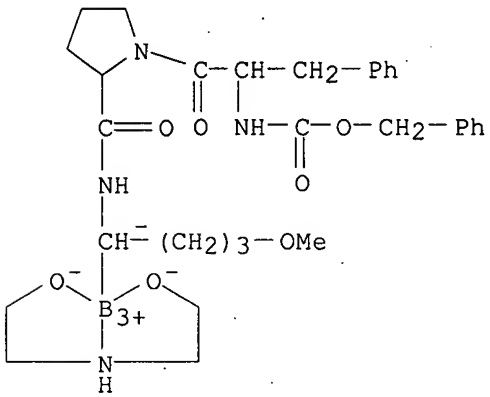
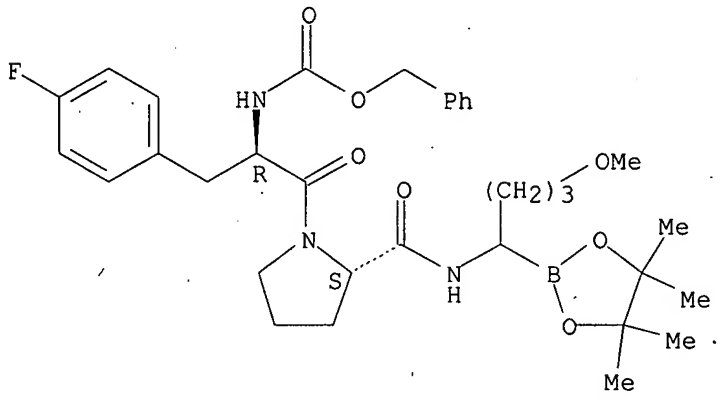
CN Boron, [[2,2'-(imino-κN)bis[ethanolato-κO]](2-)][(1S)-4-methoxy-1-[[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-D-prolyl]amino]butyl]-, (T-4)- (9CI) (CA INDEX NAME)



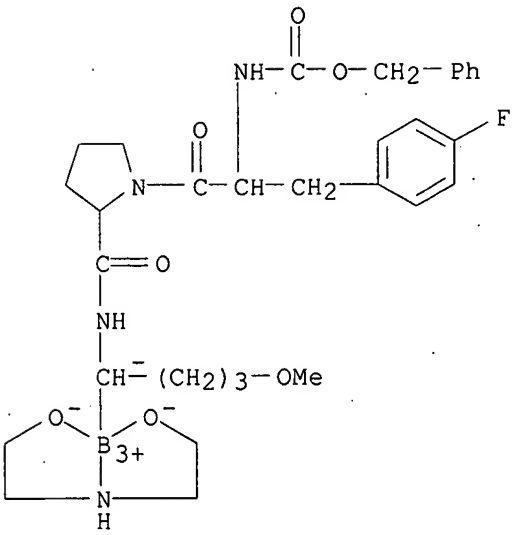
RN 864466-82-0 HCAPLUS
CN L-Prolinamide, 4-fluoro-N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[4-methoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



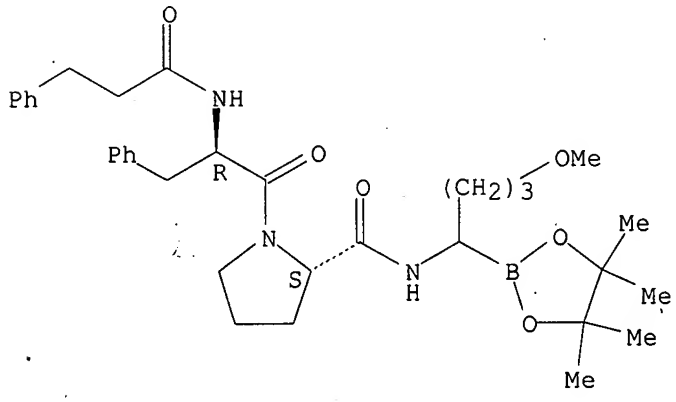
RN 864466-83-1 HCAPLUS
CN Boron, [(1R)-1-[[4-fluoro-N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-L-prolyl]amino]-4-methoxybutyl-κC][[2,2'-(imino-

κN)bis[ethanolato-κO]](2-)]-, (T-4)- (9CI) (CA INDEX NAME)



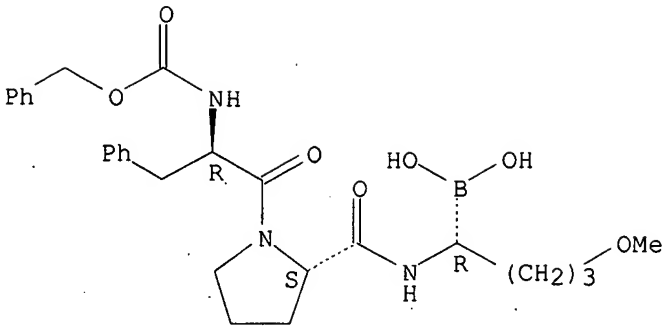
RN 864466-93-3 HCAPLUS
CN L-Prolinamide, N-(1-oxo-3-phenylpropyl)-D-phenylalanyl-N-[4-methoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 871576-03-3 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-1-borono-4-methoxybutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:735303 HCAPLUS
DOCUMENT NUMBER: 143:173146
ENTRY DATE: Entered STN: 12 Aug 2005
TITLE: Preparation of peptide boronic acid salts for use in anti-thrombotic pharmaceutical formulations
INVENTOR(S): Madge, David Jonathan; Dolman, Mark; Walter, Armin; Krimmer, Dieter; Deadman, John Joseph; Olbrich, Alfred; Weiland-Waibel, Andrea M. t.
PATENT ASSIGNEE(S): Trigen Limited, UK
SOURCE: U.S. Pat. Appl. Publ., 65 pp., Cont.-in-part of U.S. Ser. No. 659,179.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K038-04
SECONDARY: A61K031-69; C07K005-04; C07F005-02
US PATENT CLASSIF.: 514019000; 514064000; 548405000
CLASSIFICATION: 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 29, 63
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 2005176651	A1	20050811	US 2004-937854	20040908	<--
AU 2003263328	A1	20040329	AU 2003-263328	20030909	
AU 2003263333	A1	20040329	AU 2003-263333	20030909	
AU 2003263343	A1	20040329	AU 2003-263343	20030909	
US 2004138175	A1	20040715	US 2003-658971	20030909	<--
US 2004147453	A1	20040729	US 2003-659179	20030909	
EP 1466916	A1	20041013	EP 2004-76510	20030909	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
EP 1466917	A1	20041013	EP 2004-76521	20030909	
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BR 2003014518	A	20050726	BR 2003-14518	20030909	
EP 1561466	A2	20050810	EP 2004-76548	20030909	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2005288253	A1	20051229	US 2003-659178	20030909	

JP 2006503903	T2	20060202	JP 2004-569794		20030909
US 2005282757	A1	20051222	US 2005-78097		20050309 <--
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			GB 2002-20822	A	20020909
			GB 2003-7817	A	20030404
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			WO 2003-GB3883	W	20030909
			WO 2003-GB3887	W	20030909
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			US 2004-937181	A2	20040908
			US 2004-937854	A2	20040908

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2005176651	ICM	A61K038-04
	ICS	A61K031-69; C07K005-04; C07F005-02
	INCL	514019000; 514064000; 548405000
	IPCI	A61K0038-04 [ICM,7]; A61K0031-69 [ICS,7]; C07K0005-04 [ICS,7]; C07F0005-02 [ICS,7]
	IPCR	A61K0031-69 [I,A]; A61K0031-69 [I,C]; A61K0038-04 [I,A]; A61K0038-04 [I,C]; C07F0005-00 [I,C]; C07F0005-02 [I,A]; C07K0005-00 [I,C]; C07K0005-04 [I,A]
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AU 2003263328	IPCI	A61K0031-69 [ICM,7]; C07F0005-02 [ICS,7]; C07D0207-08 [ICS,7]
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US 2004138175	IPCI	A61K0031-69 [ICM,7]
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	NCL	514/019.000
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	ECLA	A61K031/69; C07F005/02C; C07K005/06A2+H; C07K005/06T
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	ECLA	A61K031/69; C07F005/02C; C07K005/06A2+H; C07K005/06T
BR 2003014450	IPCI	A61K0031-69 [ICM,7]; C07F0005-02 [ICS,7]; C07D0207-08 [ICS,7]
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BR 2003014518	IPCI	A61K0031-69 [ICM,7]; C07F0005-02 [ICS,7]; C07D0207-08 [ICS,7]
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	ECLA	A61K031/69; C07F005/02C; C07K005/06A2+H; C07K005/06T

US 2005288253 IPCI C07F0005-02 [ICM,7]; A61K0031-69 [ICS,7]
NCL 514/064.000; 562/007.000
JP 2006503903 IPCI C07K0005-06 [I,A]; A61K0009-48 [I,A]; A61K0045-00 [I,A]; A61P0007-02 [I,A]; A61P0009-10 [I,A]; A61P0013-12 [I,A]; A61P0043-00 [I,A]; C07K0005-065 [I,A]; A61K0038-00 [I,A]; C12N0009-99 [N,A]
FTERM 4C076/AA45; 4C076/AA60; 4C076/AA94; 4C076/AA95; 4C076/BB01; 4C076/CC11; 4C076/CC14; 4C076/CC17; 4C076/EE42; 4C076/FF24; 4C076/FF27; 4C076/FF31; 4C084/AA02; 4C084/AA03; 4C084/AA06; 4C084/AA07; 4C084/AA19; 4C084/BA14; 4C084/BA23; 4C084/BA33; 4C084/CA59; 4C084/DC35; 4C084/MA52; 4C084/NA14; 4C084/ZA36; 4C084/ZA54; 4C084/ZA81; 4C084/ZC20; 4H045/AA10; 4H045/AA20; 4H045/AA30; 4H045/BA11; 4H045/BA50; 4H045/DA56; 4H045/EA24; 4H045/FA10; 4H045/GA05
US 2005282757 IPCI A61K0038-05 [ICM,7]; A61K0031-69 [ICS,7]
NCL 514/018.000; 514/064.000 <--

OTHER SOURCE(S): MARPAT 143:173146

ABSTRACT:
The invention relates to tripeptide boronic acids of (R,S,R) configuration, e.g., Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)2 (TRI 50c; Mpg = 3-methoxypropylglycine residue; Cbz = benzyloxycarbonyl), and their use to make base addition salts which are formulated into anti-thrombotic pharmaceutical formulations. Thus, TRI 50c pinacol ester and magnesium salt were prepared and their activities in a thrombin amidolytic assay shown in a figure. TRI 50c and novel products of the invention are effective in arterial as well as venous contexts.

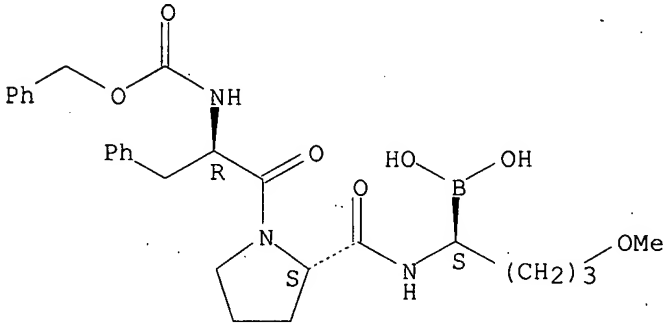
SUPPL. TERM: peptide boronic acid prepn antithrombotic
INDEX TERM: Tripeptides
ROLE: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(boronic; preparation of peptide boronic acid salts for use in anti-thrombotic pharmaceutical formulations)
INDEX TERM: Anticoagulants
Thrombosis
(preparation of peptide boronic acid salts for use in anti-thrombotic pharmaceutical formulations)
INDEX TERM: 9002-04-4, Thrombin
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of peptide boronic acid salts for use in anti-thrombotic pharmaceutical formulations)
INDEX TERM: 7440-66-6DP, Zinc, complexes with tripeptide TRI 50c
667917-15-9P 667917-16-0DP, complexes with zinc **667917-16-0P 667917-80-8P 667917-82-0P 667917-83-1P 667917-86-4P 667917-88-6P 861229-94-9P 861229-95-0P**
ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide boronic acid salts for use in anti-thrombotic pharmaceutical formulations)
INDEX TERM: 76-09-5, Pinacol 111-42-2, reactions **121-43-7** 999-97-3 17460-56-9 36215-07-3
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptide boronic acid salts for use in anti-thrombotic pharmaceutical formulations)

INDEX TERM: **162854-89-9P 162990-46-7P**
667917-13-7P 667917-14-8P
667935-30-0P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide boronic acid salts for use in anti-thrombotic pharmaceutical formulations)

IT **667917-15-9P 667917-16-0DP**, complexes with zinc
667917-16-0P 667917-80-8P 667917-82-0P
667917-83-1P 667917-86-4P 667917-88-6P
861229-94-9P 861229-95-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide boronic acid salts for use in anti-thrombotic pharmaceutical formulations)

RN 667917-15-9 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]-, calcium salt (9CI) (CA INDEX NAME)

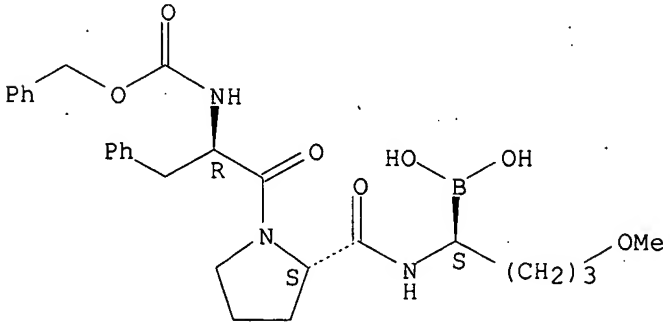
Absolute stereochemistry.



●x Ca

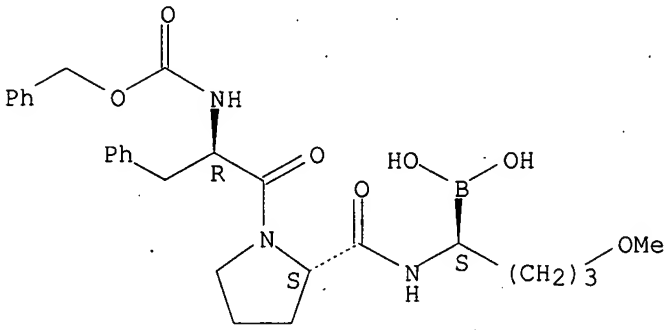
RN 667917-16-0 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



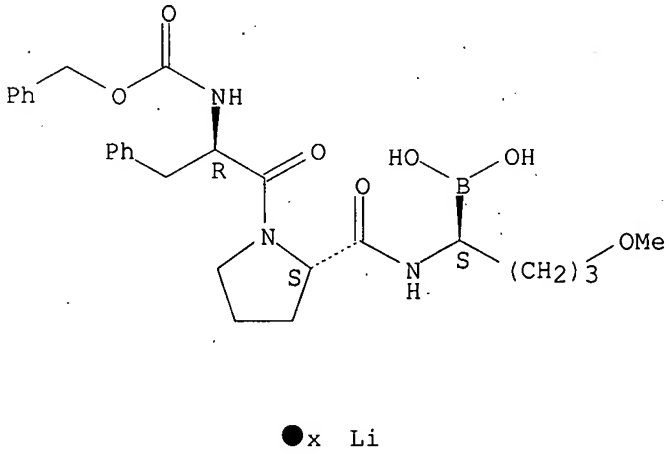
RN 667917-16-0 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 667917-80-8 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]-, lithium salt (9CI) (CA INDEX NAME)

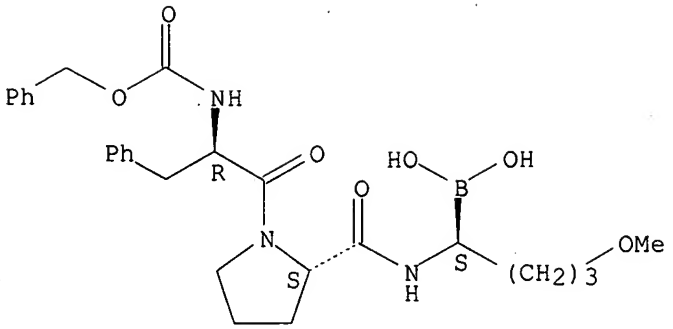
Absolute stereochemistry.



●x Li

RN 667917-82-0 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]-, sodium salt (9CI) (CA INDEX NAME)

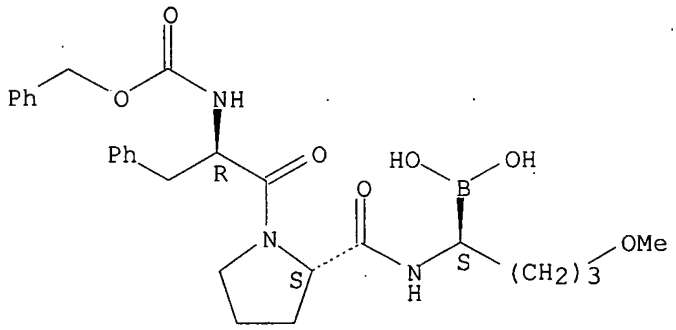
Absolute stereochemistry.



●x Na

RN 667917-83-1 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]-, potassium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



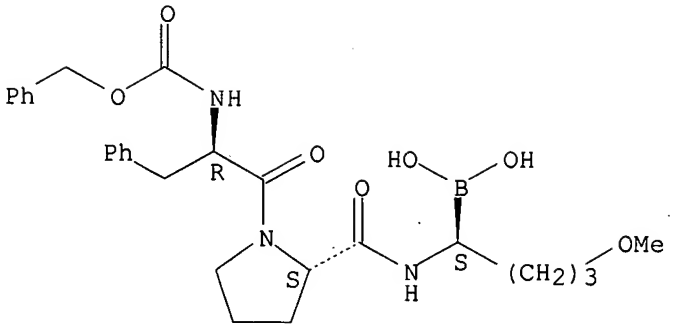
●x K

RN 667917-86-4 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]-, compd. with L-arginine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 667917-16-0
CMF C27 H36 B N3 O7

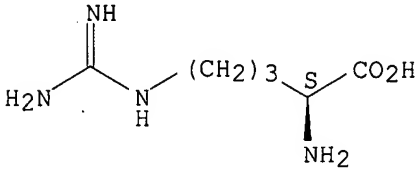
Absolute stereochemistry.



CM 2

CRN 74-79-3
CMF C6 H14 N4 O2

Absolute stereochemistry.

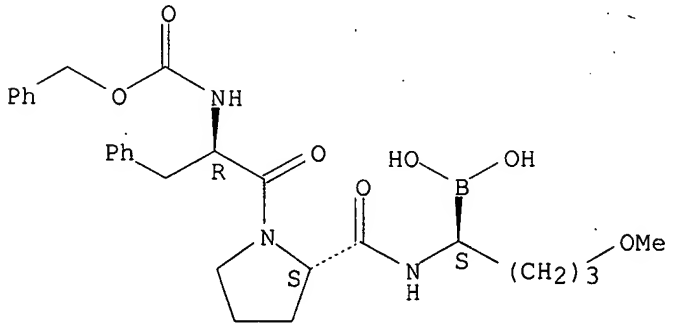


RN 667917-88-6 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]-, compd. with L-lysine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 667917-16-0
CMF C27 H36 B N3 O7

Absolute stereochemistry.

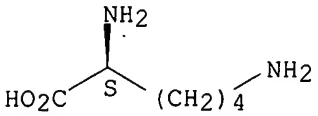


CM 2

CRN 56-87-1

CMF C6 H14 N2 O2

Absolute stereochemistry.

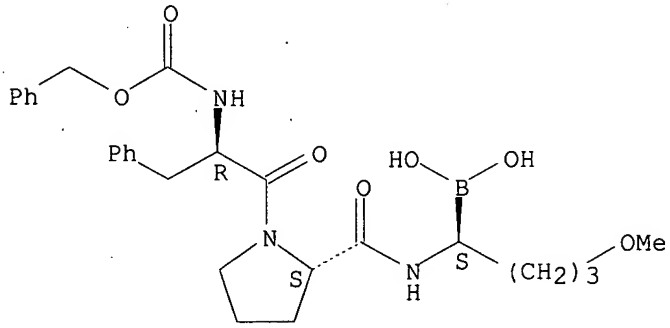


RN 861229-94-9 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]-, compd. with 1-deoxy-1-(methylamino)-D-glucitol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 667917-16-0
CMF C27 H36 B N3 O7

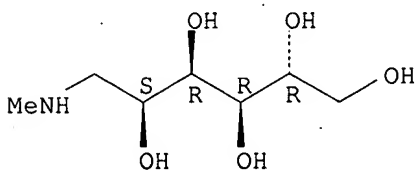
Absolute stereochemistry.



CM 2

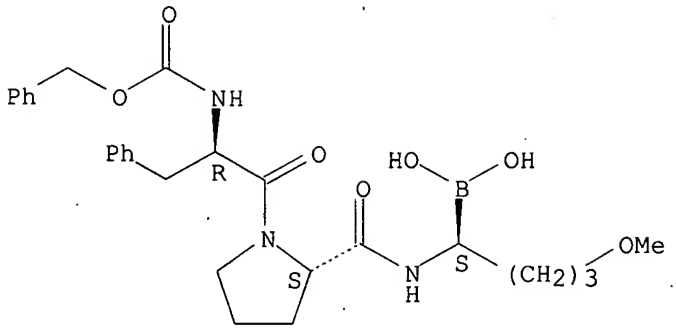
CRN 6284-40-8
CMF C7 H17 N O5

Absolute stereochemistry.



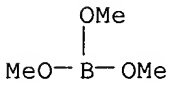
RN 861229-95-0 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]-, magnesium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

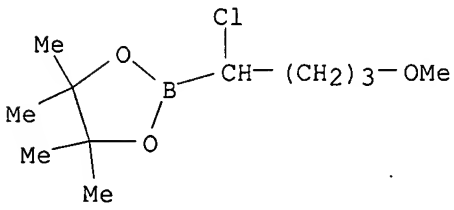


●x Mg

IT **121-43-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptide boronic acid salts for use in anti-thrombotic pharmaceutical formulations)
RN 121-43-7 HCAPLUS
CN Boric acid (H3BO3), trimethyl ester (8CI, 9CI) (CA INDEX NAME)

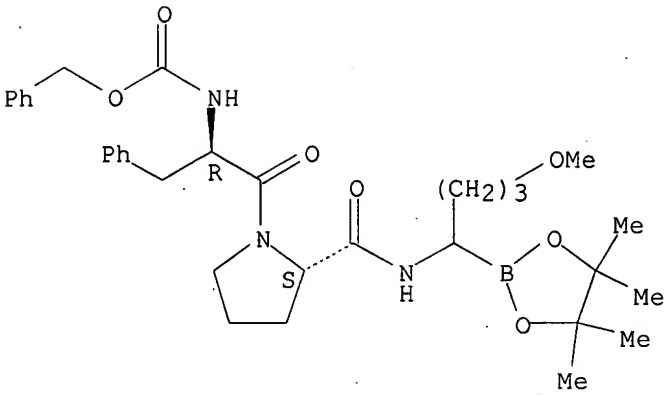


IT **162854-89-9P 162990-46-7P 667917-13-7P**
667917-14-8P 667935-30-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide boronic acid salts for use in anti-thrombotic pharmaceutical formulations)
RN 162854-89-9 HCAPLUS
CN 1,3,2-Dioxaborolane, 2-(1-chloro-4-methoxybutyl)-4,4,5,5-tetramethyl- (9CI) (CA INDEX NAME)

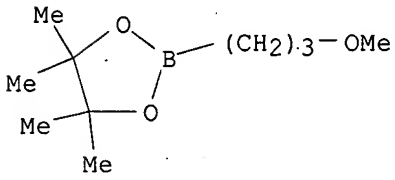


RN 162990-46-7 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[4-methoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl]- (9CI) (CA INDEX NAME)

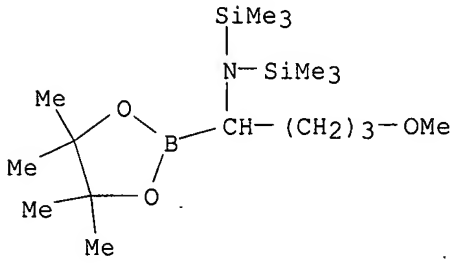
Absolute stereochemistry.



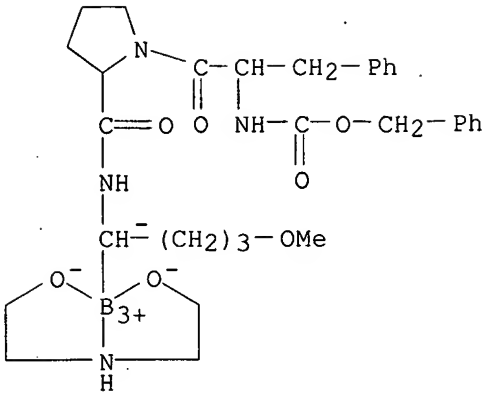
RN 667917-13-7 HCAPLUS
CN 1,3,2-Dioxaborolane, 2-(3-methoxypropyl)-4,4,5,5-tetramethyl- (9CI) (CA INDEX NAME)



RN 667917-14-8 HCAPLUS
CN 1,3,2-Dioxaborolane-2-methanamine, α-(3-methoxypropyl)-4,4,5,5-tetramethyl-N,N-bis(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 667935-30-0 HCAPLUS
CN Boron, [[2,2'-(imino-κN)bis[ethanolato-κO]](2-)][(1S)-4-methoxy-1-[[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-D-prolyl]amino]butyl]-, (T-4)- (9CI) (CA INDEX NAME)



L5 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:474929 HCAPLUS
DOCUMENT NUMBER: 143:7986
ENTRY DATE: Entered STN: 03 Jun 2005
TITLE: Method for synthesizing peptide boronic acids
INVENTOR(S): Walter, Armin; Olbrich, Alfred; Weiland-Waibel, Andrea M. T.; Krimmer, Dieter
PATENT ASSIGNEE(S): Trigen Limited, Switz.
SOURCE: U.S. Pat. Appl. Publ., 43 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07F005-02
SECONDARY: A61K031-69
US PATENT CLASSIF.: 514064000; 562007000
CLASSIFICATION: 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 29, 63
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 2005119226	A1	20050602	US 2004-937181		20040908	
US 2005282757	A1	20051222	US 2005-78097		20050309	<--
PRIORITY APPLN. INFO.:			US 2003-501718P	P	20030909	
			GB 2002-20764	A	20020909	
			GB 2002-20822	A	20020909	
			GB 2003-7817	A	20030404	
			GB 2003-11237	A	20030516	
			GB 2003-15691	A	20030704	
			US 2003-658971	A2	20030909	<--
			US 2003-659178	A2	20030909	
			US 2003-659179	A2	20030909	
			US 2004-937181	A2	20040908	
			US 2004-937854	A2	20040908	

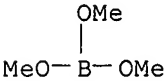
PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2005119226	ICM	C07F005-02
	ICS	A61K031-69
	INCL	514064000; 562007000

IPCI C07F0005-02 [ICM,7]; A61K0031-69 [ICS,7]
IPCR C07F0005-00 [I,C]; C07F0005-02 [I,A]
NCL 514/064.000
ECLA C07F005/02C
US 2005282757 IPCI A61K0038-05 [ICM,7]; A61K0031-69 [ICS,7]
NCL 514/018.000; 514/064.000 <--
OTHER SOURCE(S): MARPAT 143:7986
ABSTRACT:
Organoboronic acids, e.g., Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)2 (Mpg = 3-methoxypropylglycine residue; Cbz = benzyloxycarbonyl), are made by hydrolyzing their diethanolamine adducts under conditions which avoid substantial C-B bond breakage. The product acids are substantially free of degradation product derived from cleavage of the C-B bond and are converted into base addition salts for use in anti-thrombotic pharmaceutical formulations.

SUPPL. TERM: peptide boronic acid prepn antithrombotic
INDEX TERM: Peptides, preparation
ROLE: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(boronic; synthesis of peptide boronic acids via cleavage of diethanolamine adducts)
INDEX TERM: Anticoagulants
Thrombosis
(synthesis of peptide boronic acids via cleavage of diethanolamine adducts)
INDEX TERM: 76-09-5, Pinacol 111-42-2, Diethanolamine, reactions **121-43-7**, Trimethyl borate 999-97-3, Hexamethyldisilazane 17460-56-9, Cbz D phe pro oh 36215-07-3, 1-Chloro-3-methoxypropane
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of peptide boronic acids via cleavage of diethanolamine adducts)
INDEX TERM: **162854-89-9P 162990-46-7P 667917-13-7P 667917-14-8P 667935-30-0P**
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of peptide boronic acids via cleavage of diethanolamine adducts)
INDEX TERM: **667917-15-9P 667917-16-0P 667917-82-0P 852457-84-2P**
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of peptide boronic acids via cleavage of diethanolamine adducts)

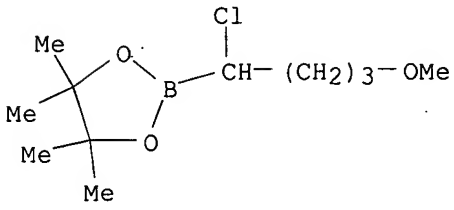
IT **121-43-7**, Trimethyl borate
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of peptide boronic acids via cleavage of diethanolamine adducts)
RN 121-43-7 HCAPLUS
CN Boric acid (H3BO3), trimethyl ester (8CI, 9CI) (CA INDEX NAME)



IT **162854-89-9P 162990-46-7P 667917-13-7P 667917-14-8P 667935-30-0P**

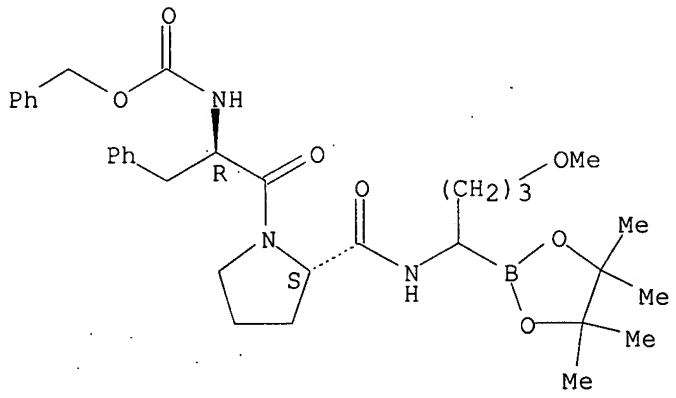
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of peptide boronic acids via cleavage of diethanolamine adducts)

RN 162854-89-9 HCAPLUS
CN 1,3,2-Dioxaborolane, 2-(1-chloro-4-methoxybutyl)-4,4,5,5-tetramethyl- (9CI) (CA INDEX NAME)

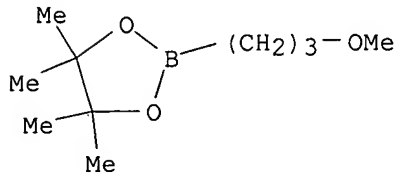


RN 162990-46-7 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[4-methoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl]- (9CI) (CA INDEX NAME)

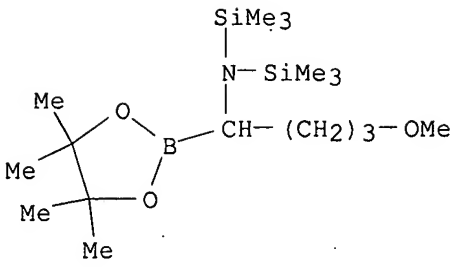
Absolute stereochemistry.



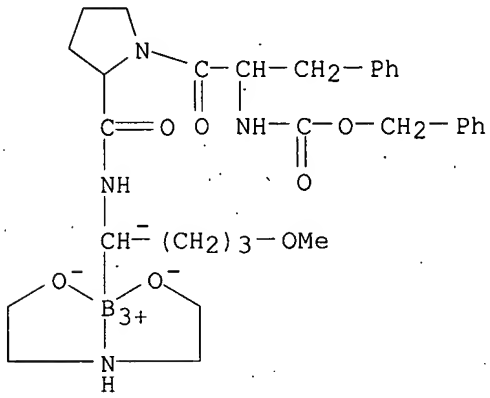
RN 667917-13-7 HCAPLUS
CN 1,3,2-Dioxaborolane, 2-(3-methoxypropyl)-4,4,5,5-tetramethyl- (9CI) (CA INDEX NAME)



RN 667917-14-8 HCAPLUS
CN 1,3,2-Dioxaborolane-2-methanamine, α-(3-methoxypropyl)-4,4,5,5-tetramethyl-N,N-bis(trimethylsilyl)- (9CI) (CA INDEX NAME)

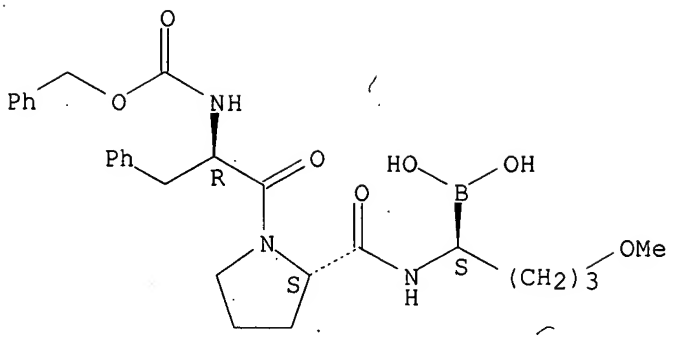


RN 667935-30-0 HCAPLUS
CN Boron, [[2,2'-(imino-κN)bis[ethanolato-κO]](2-)][(1S)-4-methoxy-1-[[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-D-prolyl]amino]butyl]-, (T-4)- (9CI) (CA INDEX NAME)



IT **667917-15-9P 667917-16-0P 667917-82-0P 852457-84-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of peptide boronic acids via cleavage of diethanolamine adducts)
RN 667917-15-9 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]-, calcium salt (9CI) (CA INDEX NAME)

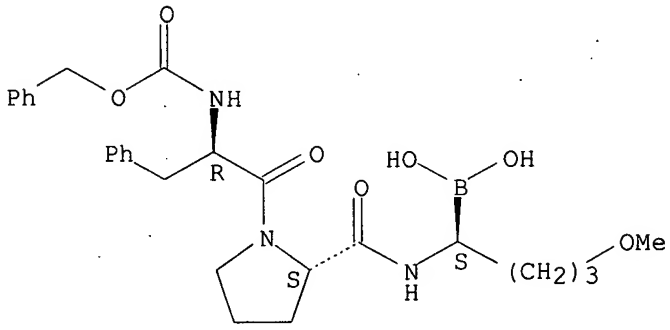
Absolute stereochemistry.



●x Ca

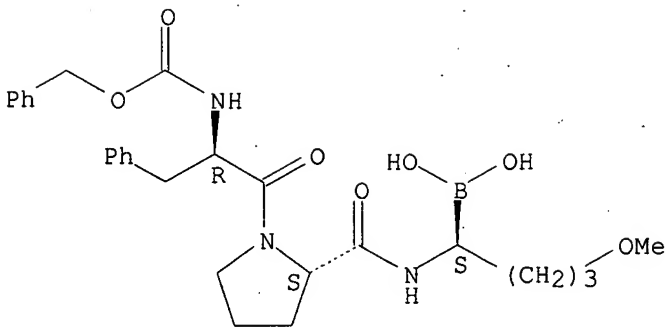
RN 667917-16-0 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 667917-82-0 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]-, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● x Na

RN 852457-84-2 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-[(1S)-1-borono-4-methoxybutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.